

36. **PRELIMINARY INSIGHTS INTO JWH182: A SYNTHETIC CANNABINOID'S NEUROPROTECTIVE ROLE AGAINST PACLITAXEL-INDUCED NEURONAL TOXICITY**

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 <https://www.youtube.com/watch?v=vlsNiqV1-28&t=12459s>

BACKGROUND: Chemotherapy-induced peripheral neuropathy (CIPN), a frequently encountered consequence of neurotoxic chemotherapy, affects approximately 30 to 40% of patients. Taxanes are associated with an exceptionally high incidence of peripheral neuropathy, with Paclitaxel (PTX) accounting for approximately 70,8% of CIPN cases. Patient's symptoms are severe, compelling oncologists to consider dosage reduction or even complete abandonment of the treatment plan. Several recent studies have shown the potential efficacy of either synthetic, endogenous or phytocannabinoids in alleviating CIPN symptoms. In case of in vitro studies, neural protection can be assessed by measuring the axon length of the cultured neurons. Therefore, our study aimed to investigate whether the synthetic cannabinoid JWH182 could emerge as a promising new candidate for managing Paclitaxel-induced peripheral neuropathy, in case of an in vitro neural model. **METHODS:** Primary neuronal cultures were obtained from mouse-derived dorsal root ganglia (DRG) explants. The harvested ganglia were subjected to a series of enzymatic and mechanical dissociating processes, followed by a density-gradient centrifugation to isolate neurons, which were then seeded in Poly-D-Lysine coated 6-well plates and incubated for 24h. Thereafter, cells were exposed to an equal parts solution of 20 uM JWH182 and 1uM PTX. As a means of comparison, the neurons from the positive control group were exclusively exposed to a 1uM PTX solution, whereas the negative control group was left untreated. Photographs of the neurons were taken before the treatment and subsequently at 6, 24, 48 and 72 hours, with a particular focus on observing changes in axon length and cell viability. **RESULTS:** Unlike our positive control group, which displayed noticeable adverse effects on axon length, the sample treated with both PTX and JWH182 presented more promising outcomes. To be precise, there was a less important reduction in axon length at all time points following drug administration. In the meantime, the negative control exhibited no changes, maintaining a typical morphology and rate of axonal growth. **CONCLUSION:** These findings suggest that the synthetic cannabinoid JWH182 confers a protective effect on DRG neurons treated with Paclitaxel. As a result, this compound holds the potential to emerge as a novel treatment option for managing Paclitaxel-induced peripheral neuropathy. This could lead to the alleviation of symptoms in oncological patients, thereby enhancing their quality of life and their overall disease prognosis. Ultimately, these initial results lay the foundation for subsequent in vitro and in vivo experiments, aimed at validating our hypothesis.

Key words: Cannabinoids; Paclitaxel; Antineoplastic Agents / Toxicity; Peripheral Nervous System Diseases / Chemically Induced; Peripheral Nervous System Diseases / Therapy (Source: MeSH-NLM).